SEQUENCE LISTING

<110> Nicolaides, Nicholas C Sass, Philip M Grasso, Luigi M Kline, J Bradford

- <120> METHODS FOR GENERATING ANTIBIOTIC RESISTANT MICROBES AND NOVEL ANTIBIOTICS
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- <140> 00/000,000 <141> 2001-07-25
- <160> 39
- <170> PatentIn version 3.1
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Lys Leu Gln Lys Phe Glu Asp Leu Ser Gln Ile Gln Thr Tyr Gly Phe

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Val Gly Arg Tyr Ala Ile His Ser Lys Asp Ile Gly Phe Ser Cys Lys 190 180

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Ser Leu Ile Phe Phe Ile Asn Asn Arg Leu Val Thr Cys Asp Leu Leu 260 265 270

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Ile Asp Thr Ser Arg Thr Phe Lys Ala Ser Ser Ile Ser Thr Asn Lys 340 345 350

Pro Glu Ser Leu Ile Pro Phe Asn Asp Thr Ile Glu Ser Asp Arg Asn 355 \$360\$

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Arg Ile Asp Ala Ser Gln Ala Lys Ile Thr Ser Phe Leu Ser Ser Ser 405 410 415

Gln Gln Phe Asn Phe Glu Gly Ser Ser Thr Lys Arg Gln Leu Ser Glu 420 425 430

Pro Lys Val Thr Asn Val Ser His Ser Gln Glu Ala Glu Lys Leu Thr 435 440 445

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Ser Ile Lys Lys Leu Arg Glu Lys Val Asp Asp Ser Ile His Arg Glu 515 520 525

Glu Arg Arg Leu Ala Ala Ile Gln His Asp Leu Lys Leu Phe Leu Ile 545 550555555

Asp Tyr Gly Ser Val Cys Tyr Glu Leu Phe Tyr Gln Ile Gly Leu Thr 565 570 575

Asp Phe Ala Asn Phe Gly Lys Ile Asn Leu Gln Ser Thr Asn Val Ser 580 580 590

Asp Asp Ile Val Leu Tyr Asn Leu Leu Ser Glu Phe Asp Glu Leu Asn 595 600 605

Asp Asp Ala Ser Lys Glu Lys Ile Ile Ser Lys Ile Trp Asp Met Ser 610 615 620

Ser Met Leu Asn Glu Tyr Tyr Ser Ile Glu Leu Val Asn Asp Gly Leu 625 630 635 640

Asp Asn Asp Leu Lys Ser Val Lys Leu Lys Ser Leu Pro Leu Leu Leu 645 650 655

Lys Gly Tyr Ile Pro Ser Leu Val Lys Leu Pro Phe Phe Ile Tyr Arg

Leu Gly Lys Glu Val Asp Trp Glu Asp Glu Gln Glu Cys Leu Asp Gly 675 680 685

Ile Leu Arg Glu Ile Ala Leu Leu Tyr Ile Pro Asp Met Val Pro Lys 690 700

Val Asp Thr Leu Asp Ala Ser Leu Ser Glu Asp Glu Lys Ala Gln Phe 705 710 715 720

Ile Asn Arg Lys Glu His Ile Ser Ser Leu Leu Glu His Val Leu Phe

Pro Cys Ile Lys Arg Arg Phe Leu Ala Pro Arg His Ile Leu Lys Asp

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Leu Ile Glu Val Ser Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe 65 70 75 80

Glu Gly Leu Ala Leu Lys His His Thr Ser Lys Ile Gln Glu Phe Ala 85 90 95

Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg Gly Glu Ala Leu Ser 100 105 110

Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser Thr Cys His Gly Ser 115 120 125

Ala Ser Val Gly Thr Arg Leu Val Phe Asp His Asn Gly Lys Ile Thr 130 $\,$ 140

Gln Lys Thr Pro Tyr Pro Arg Pro Lys Gly Thr Thr Val Ser Val Gln 145 150 160

His Leu Phe Tyr Thr Leu Pro Val Arg Tyr Lys Glu Phe Gln Arg Asn 165 170 175

Ile Lys Lys Glu Tyr Ser Lys Met Val Gln Val Leu Gln Ala Tyr Cys 180 185 190

Ile Ile Ser Ala Gly Val Arg Val Ser Cys Thr Asn Gln Leu Gly Gln 195 200

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Phe His Ser Ala Arg Thr Ala Pro Gly Gly Val Gln Gln Thr Gly Ser 275 280 285

Phe Ser Ser Ser Ile Arg Gly Pro Val Thr Gln Gln Arg Ser Leu Ser 290 295 300

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Thr Pro Asp Lys Arg Gln Ile Leu Leu Gln Glu Glu Lys Leu Leu Leu 340 \$345\$

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Val Lys Leu His Thr Ala Glu Leu Glu Lys Pro Val Pro Gly Lys Gln 385 390 395

Asp Asn Ser Pro Ser Leu Lys Ser Thr Ala Asp Glu Lys Arg Val Ala 405 410 415

Ser Ile Ser Arg Leu Arg Glu Ala Phe Ser Leu His Pro Thr Lys Glu 420 425 430

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Leu Ser Ser Thr Ser Ala Gly Ser Glu Glu Glu Phe Ser Thr Pro Glu 500 505 510

Val Ala Ser Ser Phe Ser Ser Asp Tyr Asn Val Ser Ser Leu Glu Asp

Arg Pro Ser Gln Glu Thr Ile Asn Cys Gly Asp Leu Asp Cys Arg Pro

Pro Gly Thr Gly Gln Ser Leu Lys Pro Glu Asp His Gly Tyr Gln Cys 545 550 550 555

Lys Ala Leu Pro Leu Ala Arg Leu Ser Pro Thr Asn Ala Lys Arg Phe 565 570 575

Lys Thr Glu Glu Arg Pro Ser Asn Val Asn Ile Ser Gln Arg Leu Pro $580 \hspace{1.5cm} 585 \hspace{1.5cm} 590 \hspace{1.5cm}$

Gly Pro Gln Ser Thr Ser Ala Ala Glu Val Asp Val Ala Ile Lys Met $595 \\ $ 600 605

Asn Lys Arg Ile Val Leu Leu Glu Phe Ser Leu Ser Ser Leu Ala Lys 610 615

Arg Met Lys Gln Leu Gln His Leu Lys Ala Gln Asn Lys His Glu Leu 625 630 640

Ser Tyr Arg Lys Phe Arg Ala Lys Ile Cys Pro Gly Glu Asn Gln Ala $_{645}^{\rm C}$

Ala Glu Asp Glu Leu Arg Lys Glu Ile Ser Lys Ser Met Phe Ala Glu 660 660 660

Met Glu Ile Leu Gly Gln Phe Asn Leu Gly Phe Ile Val Thr Lys Leu 675 680 685

Lys Glu Asp Leu Phe Leu Val Asp Gln His Ala Ala Asp Glu Lys Tyr $_{690}$

Asn Phe Glu Met Leu Gln Gln His Thr Val Leu Gln Ala Gln Arg Leu 705 710 715 720

Ile Thr Pro Gln Thr Leu Asn Leu Thr Ala Val Asn Glu Ala Val Leu 725 $$ 730 $$ 735

Ile Glu Asn Leu Glu Ile Phe Arg Lys Asn Gly Phe Asp Phe Val Ile $740 \hspace{1.5cm} 745 \hspace{1.5cm} 750 \hspace{1.5cm}$

Asp Glu Asp Ala Pro Val Thr Glu Arg Ala Lys Leu Ile Ser Leu Pro 755 760 765

Thr Ser Lys Asn Trp Thr Phe Gly Pro Gln Asp Ile Asp Glu Leu Ile 770 775 780

Phe Met Leu Ser Asp Ser Pro Gly Val Met Cys Arg Pro Ser Arg Val 785 790 795 800

Arg Gln Met Phe Ala Ser Arg Ala Cys Arg Lys Ser Val Met Ile Gly 805 810 815

Thr Ala Leu Asn Ala Ser Glu Met Lys Lys Leu Ile Thr His Met Gly 820 825 830

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Ile Ile Thr Ser Val Val Ser Val Val Lys Glu Leu Ile Glu Asn Ser 20 25 30

Leu Asp Ala Gly Ala Thr Ser Val Asp Val Lys Leu Glu Asn Tyr Gly 35 40 45

Phe Asp Lys Ile Glu Val Arg Asp Asn Gly Glu Gly Ile Lys Ala Val 50 $\,$

Asp Ala Pro Val Met Ala Met Lys Tyr Tyr Thr Ser Lys Ile Asn Ser 65 70 75 80

His Glu Asp Leu Glu Asn Leu Thr Thr Tyr Gly Phe Arg Gly Glu Ala 85 90 90

Leu Gly Ser Ile Cys Cys Ile Ala Glu Val Leu Ile Thr Thr Arg Thr

Ala Ala Asp Asn Phe Ser Thr Gln Tyr Val Leu Asp Gly Ser Gly His 115 \$120\$

Ile Leu Ser Gln Lys Pro Ser His Leu Gly Gln Gly Thr Thr Val Thr 130 135 140

Ala Leu Arg Leu Phe Lys Asn Leu Pro Val Arg Lys Gln Phe Tyr Ser 145 $$ 150 $$ 155 $$ 160

Thr Ala Lys Lys Cys Lys Asp Glu Ile Lys Lys Ile Gln Asp Leu Leu 165 170 175

Met Ser Phe Gly Ile Leu Lys Pro Asp Leu Arg Ile Val Phe Val His

Asn Lys Ala Val Ile Trp Gln Lys Ser Arg Val Ser Asp His Lys Met 195 200 205

Ala Leu Met Ser Val Leu Gly Thr Ala Val Met Asn Asn Met Glu Ser 210 215 220

465

Phe Gln Tyr His Ser Glu Glu Ser Gin Ile Tyr Leu Ser Gly Phe Leu 225 Pro Lvs Cvs Asp Ala Asp His Ser Phe Thr Ser Leu Ser Thr Pro Glu Arg Ser Phe Ile Phe Ile Asn Ser Arg Pro Val His Gln Lys Asp Ile 260 265 270 Leu Lys Leu Ile Arg His His Tyr Asn Leu Lys Cys Leu Lys Glu Ser 275 Thr Arg Leu Tyr Pro Val Phe Phe Leu Lys Ile Asp Val Pro Thr Ala 290 295 Asp Val Asp Val Asn Leu Thr Pro Asp Lys Ser Gln Val Leu Leu Gln 305 310 Asn Lys Glu Ser Val Leu Ile Ala Leu Glu Asn Leu Met Thr Thr Cys Tyr Glv Pro Leu Pro Ser Thr Asn Ser Tyr Glu Asn Asn Lys Thr Asp 345 Val Ser Ala Ala Asp Ile Val Leu Ser Lys Thr Ala Glu Thr Asp Val Leu Phe Asn Lys Val Glu Ser Ser Gly Lys Asn Tyr Ser Asn Val Asp Thr Ser Val Ile Pro Phe Gln Asn Asp Met His Asn Asp Glu Ser Gly Lys Asn Thr Asp Asp Cys Leu Asn His Gln Ile Ser Ile Gly Asp Phe Gly Tyr Gly His Cys Ser Ser Glu Ile Ser Asn Ile Asp Lys Asn Thr 420 425 Lys Asn Ala Phe Gln Asp Ile Ser Met Ser Asn Val Ser Trp Glu Asn 435 Ser Gln Thr Glu Tyr Ser Lys Thr Cys Phe Ile Ser Ser Val Lys His 450 455 Thr Gln Ser Glu Asn Gly Asn Lys Asp His Ile Asp Glu Ser Gly Glu Asn Glu Glu Glu Ala Gly Leu Glu Asn Ser Ser Glu Ile Ser Ala Asp 485 490 495

Glu Trp Ser Arg Gly Asn Ile Leu Lys Asn Ser Val Gly Glu Asn Ile 500 505 510

Glu Pro Val Lys Ile Leu Val Pro Glu Lys Ser Leu Pro Cys Lys Val 515 520 525

Ser Asn Asn Asn Tyr Pro Ile Pro Glu Gln Met Asn Leu Asn Glu Asp 530 540

Ser Cys Asn Lys Lys Ser Asn Val Ile Asp Asn Lys Ser Gly Lys Val 545 550 560

Thr Ala Tyr Asp Leu Leu Ser Asn Arg Val Ile Lys Lys Pro Met Ser 565 570 575

Ala Ser Ala Leu Phe Val Gln Asp His Arg Pro Gln Phe Leu Ile Glu 580 585 590

Asn Pro Lys Thr Ser Leu Glu Asp Ala Thr Leu Gln Ile Glu Glu Leu 595 $\,$ 600 $\,$ 605

Trp Lys Thr Leu Ser Glu Glu Glu Lys Leu Lys Tyr Glu Glu Lys Ala 610 $\,$ 620 $\,$

Thr Lys Asp Leu Glu Arg Tyr Asn Ser Gln Met Lys Arg Ala Ile Glu 625 $$ 630 $$ 630 $$ 640

Thr Ser Ala Trp Asn Leu Ala Gln Lys His Lys Leu Lys Thr Ser Leu

Ser Asn Gln Pro Lys Leu Asp Glu Leu Leu Gln Ser Gln Ile Glu Lys 675 680 685

Arg Arg Ser Gln Asn Ile Lys Met Val Gln Ile Pro Phe Ser Met Lys 690 695 700

Asn Leu Lys Ile Asn Phe Lys Lys Gln Asn Lys Val Asp Leu Glu Glu 705 710 715 720

Lys Asp Glu Pro Cys Leu Ile His Asn Leu Arg Phe Pro Asp Ala Trp $725 \hspace{1cm} 730 \hspace{1cm} 735$

Leu	Met	Thr	Ser 740	Lys	Thr	Glu	Val	Met 745	Leu	Leu	Asn	Pro	Tyr 750	Arg	Val
Glu	Glu	Ala 755	Leu	Leu	Phe	Lys	Arg 760	Leu	Leu	Glu	Asn	His 765	Lys	Leu	Pro
Ala	Glu 770	Pro	Leu	Glu	Lys	Pro 775	Ile	Met	Leu	Thr	Glu 780	Ser	Leu	Phe	Asn
31y 785	Ser	His	Tyr	Leu	Asp 790	Val	Leu	Tyr	Lys	Met 795	Thr	Ala	Asp	Asp	Gln 800
Arg	Tyr	Ser	Gly	Ser 805	Thr	Tyr	Leu	Ser	Asp 810	Pro	Arg	Leu	Thr	Ala 815	Asn
Gly	Phe	Lys	Ile 820	Lys	Leu	Ile	Pro	Gly 825	Val	Ser	Ile		Glu 830	Asn	Tyr
Leu	Glu	Ile 835	Glu	Gly	Met	Ala	Asn 840	Cys	Leu	Pro	Phe	Tyr 845	Gly	Val	Ala
Asp	Leu 850	Lys	Glu	Ile	Leu	Asn 855	Ala	Ile	Leu	Asn	Arg 860	Asn	Ala	Lys	Glu
Val 865	Tyr	Glu	Суз	Arg	Pro 870	Arg	Lys	Val	Ile	Ser 875	Tyr	Leu	Glu	Gly	Glu 880
Ala	Val	Arg	Leu	Ser 885	Arg	Gln	Leu	Pro	Met 890	Tyr	Leu	Ser	Lys	Glu 895	Asp
Ile	Gln	Asp	Ile 900	Ile	Tyr	Arg	Met	Lys 905	His	Gln	Phe	Gly	Asn 910	Glu	Ile
Lys	Glu	Cys 915	Val	His	Gly	Arg	Pro 920	Phe	Phe	His	His	Leu 925	Thr	Tyr	Leu
Pro	Glu 930	Thr	Thr												
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ctg	ctct	gtt .	aaaa	gcga	aa a	tgaa	acaa	t tg	cctg	cggc	aac	agtt	cga	ctcc	tttcaa
	at a s	~~ t	aa+a	20++	~~ ~	+ 00+	aaat	~ ++	~+ a a	2202	aat	+ > + +	~==	22Ct	acttaa

60 120 180 atgctggtgc cacaagcgta gatgttaaac tggagaacta tggatttgat aaaattgagg 240 tgegagataa eggggagggt atcaaggetg ttgatgeace tgtaatggea atgaagtaet 300 acacctcaaa aataaatagt catgaagatc ttgaaaattt gacaacttac ggttttcgtg 360 gagaagcctt ggggtcaatt tgttgtatag ctgaggtttt aattacaaca agaacggctg 420 ctgataattt tagcacccag tatgttttag atggcagtgg ccacatactt tctcagaaac 480 cttcacatct tggtcaaggt acaactgtaa ctgctttaag attatttaag aatctacctg 540 taagaaagca gttttactca actgcaaaaa aatgtaaaga tgaaataaaa aagatccaag 600 atctcctcat gagetttggt atccttaaac etgacttaag gattgtcttt gtacataaca 660 aggcagttat ttggcagaaa agcagagtat cagatcacaa gatggctctc atgtcagttc 720 tggggactgc tgttatgaac aatatggaat cctttcagta ccactctgaa gaatctcaga 780 tttatctcag tggatttctt ccaaagtgtg atgcagacca ctctttcact agtctttcaa 840 caccagaaag aagttteate tteataaaca gtegaccagt acatcaaaaa gatatettaa 900 960 agttaatccg acatcattac aatctgaaat gcctaaagga atctactcgt ttgtatcctg ttttctttct gaaaatcgat gttcctacag ctgatgttga tgtaaattta acaccagata 1020 1080 aaaqccaaqt attattacaa aataaggaat ctgttttaat tgctcttgaa aatctgatga cgacttgtta tggaccatta cctagtacaa attettatga aaataataaa acagatgttt 1140 1200 ccgcagctga catcgttctt agtaaaacag cagaaacaga tgtgcttttt aataaagtgg 1260 tgcataatga tgaatctgga aaaaacactg atgattgttt aaatcaccag ataagtattg 1320 1380 gtgactttgg ttatggtcat tgtagtagtg aaatttctaa cattgataaa aacactaaga atgcatttca ggacatttca atgagtaatg tatcatggga gaactetcag acggaatata 1440 1500 gtaaaacttg ttttataagt tccgttaagc acacccagtc agaaaatggc aataaagacc atatagatga gagtggggaa aatgaggaag aagcaggtet tgaaaactet teggaaattt 1560 ctgcagatga gtggagcagg ggaaatatac ttaaaaaattc agtgggagag aatattgaac 1620 ctgtgaaaat tttagtgcct gaaaaaagtt taccatgtaa agtaagtaat aataattatc 1680 caatccctga acaaatgaat cttaatgaag attcatgtaa caaaaaatca aatgtaatag 1740 ataataaatc tggaaaagtt acagcttatg atttacttag caatcgagta atcaagaaac 1800 1860 ccatgtcagc aagtgctctt tttgttcaag atcatcgtcc tcagtttctc atagaaaatc ctaagactag tttagaggat gcaacactac aaattgaaga actgtggaag acattgagtg 1920 1980 aagaggaaaa actgaaatat gaagagaagg ctactaaaga cttggaacga tacaatagtc 2040 aaatgaagag agccattgaa caggagtcac aaatgtcact aaaagatggc agaaaaaaga 2100 taaaacccac cagegcatgg aatttggccc agaagcacaa gttaaaaacc tcattatcta

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CZIJO NOMO SAPIENS

<400> 8

Met Lys Gln Leu Pro Ala Ala Thr Val Arg Leu Leu Ser Ser Gln 1 $$ 5 $$ 10 $$ 15

Ile Ile Thr Ser Val Val Ser Val Val Lys Glu Leu Ile Glu Asn Ser 20 25 30

Leu Asp Ala Gly Ala Thr Ser Val Asp Val Lys Leu Glu Asn Tyr Gly 35 40 45

Phe Asp Lys Ile Glu Val Arg Asp Asn Gly Glu Gly Ile Lys Ala Val 50 55 60

Asp Ala Pro Val Met Ala Met Lys Tyr Tyr Thr Ser Lys Ile Asn Ser 65 70 75 80

His Glu Asp Leu Glu Asn Leu Thr Thr Tyr Gly Phe Arg Gly Glu Ala Page 18 85 90 95 *****

Leu Gly Ser Ile Cys Cys Ile Ala Glu Val Leu Ile Thr Thr Arg Thr

Ala Ala Asp Asn Phe Ser Thr Gln Tyr Val Leu Asp Gly Ser Gly His

Ile Leu Ser Gln Lys Pro Ser His Leu Gly Gln Gly Thr Thr Val Thr 130 135 140

Ala Leu Arg Leu Phe Lys Asn Leu Pro Val Arg Lys Gln Phe Tyr Ser 145 150 155 160

Thr Ala Lys Lys Cys Lys Asp Glu Ile Lys Lys Ile Gln Asp Leu Leu 165 170 175

Met Ser Phe Gly Ile Leu Lys Pro Asp Leu Arg Ile Val Phe Val His 180 $$180\$

Asn Lys Ala Val Ile Trp Gln Lys Ser Arg Val Ser Asp His Lys Met 195 200 205

Ala Leu Met Ser Val Leu Gly Thr Ala Val Met Asn Asn Met Glu Ser 210 215 220

Phe Gln Tyr His Ser Glu Glu Ser Gln Ile Tyr Leu Ser Gly Phe Leu 225 $$ 230 $$ 235 $$ 240

Pro Lys Cys Asp Ala Asp His Ser Phe Thr Ser Leu Ser Thr Pro Glu

Arg Ser Phe Ile Phe Ile Asn Ser Arg Pro Val His Gln Lys Asp Ile 260 265 270

Leu Lys Leu Ile Arg His His Tyr Asn Leu Lys Cys Leu Lys Glu Ser 275 280 285

Thr Arg Leu Tyr Pro Val Phe Phe Leu Lys Ile Asp Val Pro Thr Ala 290 295 300

Asp Val Asp Val Asn Leu Thr Pro Asp Lys Ser Gln Val Leu Leu Gln 305 $$ 310 $$ 315 $$ 320

Asn Lys Glu Ser Val Leu Ile Ala Leu Glu Asn Leu Met Thr Thr Cys 325 330 335

Tyr Gly Pro Leu Pro Ser Thr Asn Ser Tyr Glu Asn Asn Lys Thr Asp Page 19 340 345 350

Val Ser Ala Ala Asp Ile Val Leu Ser Lys Thr Ala Glu Thr Asp Val

Leu Phe Asn Lys Val Glu Ser Ser Gly Lys Asn Tyr Ser Asn Val Asp 370 375 380

Thr Ser Val Ile Pro Phe Gln Asn Asp Met His Asn Asp Glu Ser Gly 385 390 395 400

Lys Asn Thr Asp Asp Cys Leu Asn His Gln Ile Ser Ile Gly Asp Phe 405 415

Gly Tyr Gly His Cys Ser Ser Glu Ile Ser Asn Ile Asp Lys Asn Thr 420 425 430

Lys Asn Ala Phe Gln Asp Ile Ser Met Ser Asn Val Ser Trp Glu Asn $435 \hspace{1.5cm} 440 \hspace{1.5cm} 445 \hspace{1.5cm}$

Ser Gln Thr Glu Tyr Ser Lys Thr Cys Phe Ile Ser Ser Val Lys His 450 455 460

Thr Gln Ser Glu Asn Gly Asn Lys Asp His Ile Asp Glu Ser Gly Glu 465 470 480

Asn Glu Glu Glu Ala Gly Leu Glu Asn Ser Ser Glu Ile Ser Ala Asp 485 490 495

Glu Trp Ser Arg Gly Asn Ile Leu Lys Asn Ser Val Gly Glu Asn Ile
500 505 510

Glu Pro Val Lys Ile Leu Val Pro Glu Lys Ser Leu Pro Cys Lys Val

Ser Asn Asn Asn Tyr Pro Ile Pro Glu Gln Met Asn Leu Asn Glu Asp 530 540

Ser Cys Asn Lys Lys Ser Asn Val Ile Asp Asn Lys Ser Gly Lys Val 545 555 560

Thr Ala Tyr Asp Leu Leu Ser Asn Arg Val Ile Lys Lys Pro Met Ser 565 570 575

Ala Ser Ala Leu Phe Val Gln Asp His Arg Pro Gln Phe Leu Ile Glu

Asn Pro Lys Thr Ser Leu Glu Asp Ala Thr Leu Gln Ile Glu Glu Leu
Page 20

595 600 605

Trp Lys Thr Leu Ser Glu Glu Glu Lys Leu Lys Tyr Glu Glu Lys Ala 610 615 620

Thr Lys Asp Leu Glu Arg Tyr Asn Ser Gln Met Lys Arg Ala Ile Glu 625 630 635

Gln Glu Ser Gln Met Ser Leu Lys Asp Gly Arg Lys Lys Ile Lys Pro 645 650 655

Thr Ser Ala Trp Asn Leu Ala Gln Lys His Lys Leu Lys Thr Ser Leu 660 665 670

Ser Asn Gln Pro Lys Leu Asp Glu Leu Leu Gln Ser Gln Ile Glu Lys 675 680 685

Arg Arg Ser Gln Asn Ile Lys Met Val Gln Ile Pro Phe Ser Met Lys $690 \hspace{1.5cm} 695 \hspace{1.5cm} 700 \hspace{1.5cm}$

Asn Leu Lys Ile Asn Phe Lys Lys Gln Asn Lys Val Asp Leu Glu Glu 705 710715 710 720

Leu Met Thr Ser Lys Thr Glu Val Met Leu Leu Asn Pro Tyr Arg Val 740 745 750

Glu Glu Ala Leu Leu Phe Lys Arg Leu Leu Glu Asn His Lys Leu Pro

Ala Glu Pro Leu Glu Lys Pro Ile Met Leu Thr Glu Ser Leu Phe Asn 770 780

Gly Ser His Tyr Leu Asp Val Leu Tyr Lys Met Thr Ala Asp Asp Gln 785 790 795 800

Arg Tyr Ser Gly Ser Thr Tyr Leu Ser Asp Pro Arg Leu Thr Ala Asn $805 \\ 810 \\ 815$

Gly Phe Lys Ile Lys Leu Ile Pro Gly Val Ser Ile Thr Glu Asn Tyr 820 825 830

Leu Glu Ile Glu Gly Met Ala Asn Cys Leu Pro Phe Tyr Gly Val Ala 835 840 845

Asp Leu Lys Glu Ile Leu Asn Ala Ile Leu Asn Arg Asn Ala Lys Glu Page 21 850 855 860

Val Tyr Glu Cys Arg Pro Arg Lys Val Ile Ser Tyr Leu Glu Gly Glu 865 870 875 880

Ala Val Arg Leu Ser Arg Gln Leu Pro Met Tyr Leu Ser Lys Glu Asp 885 890 895

Ile Gln Asp Ile Ile Tyr Arg Met Lys His Gln Phe Gly Asn Glu Ile 900 905 910

Lys Glu Cys Val His Gly Arg Pro Phe Phe His His Leu Thr Tyr Leu 915 920 925

Pro Glu Thr Thr 930

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atat	tta	gta a	tatt	ttac	t tt	gagg	acat	ttt	caaa	gat	ttt	attt	tg a	aaaa	tgaga
gcto	gtaa	ctg a	iggad	etgtt	t go	aatt	gaca	tag	gcaa	taa	taag	tgat	gt g	ctga	atttt
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Thr	Val	Arg 35	Leu	Phe	Asp	Arg	Gly 40	Asp	Phe	Tyr	Thr	Ala 45	His	Gly	Glu
Asp	Ala 50	Leu	Leu	Ala	Ala	Arg 55	Glu	Val	Phe	Lys	Thr 60	Gln	Gly	Val	Ile
Lys 65	Tyr	Met	Gly	Pro	Ala 70	Gly	Ala	Lys	Asn	Leu 75	Gln	Ser	Val	Val	Leu 80
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Gln	Tyr	Arg	Val 100	Glu	Val	Tyr	Lys	Asn 105	Arg	Ala	Gly	Asn	Lys 110	Ala	Ser
Lys	Glu	Asn 115	Asp	Trp	Tyr	Leu	Ala 120	Tyr	Lys	Ala	Ser	Pro 125	Gly	Asn	Leu
Ser	Gln 130	Phe	Glu	Asp	Ile	Leu 135	Phe	Gly	Asn	Asn	Asp 140	Met	Ser	Ala	Ser
Ile 145	Gly	Val	Val	Gly	Val 150	Lys	Met	Ser	Ala	Val 155	Asp	Gly	Gln	Arg	Gln 160
Val	Gly	Val	Gly	Tyr 165	Val	Asp	Ser	Ile	Gln 170	Arg	Lys	Leu	Gly	Leu 175	Cys
Glu	Phe	Pro	Asp	Asn	Asp	Gln	Phe	Ser 185	Asn	Leu	Glu	Ala	Leu 190	Leu	Ile

3060 3120 3145 195 200 205

Asp Met Gly Lys Leu Arg Gln Ile Ile Gln Arg Gly Gly Ile Leu Ile

Thr Glu Arg Lys Lys Ala Asp Phe Ser Thr Lys Asp Ile Tyr Gln Asp 225 230 235 240

Val Leu Pro Glu Met Glu Asn Gln Val Ala Val Ser Ser Leu Ser Ala 260 265 270

Val Ile Lys Phe Leu Glu Leu Leu Ser Asp Asp Ser Asn Phe Gly Glu 275 280 285

Phe Glu Leu Thr Thr Phe Asp Phe Ser Gln Tyr Met Lys Leu Asp Ile 290 295 300

Ala Ala Val Arg Ala Leu Asn Leu Phe Gln Gly Ser Val Glu Asp Thr 305 \$310\$

Thr Gly Ser Gln Ser Leu Ala Ala Leu Leu Asn Lys Cys Lys Thr Pro 325 330 335

Gln Gly Gln Arg Leu Val Asn Gln Trp Ile Lys Gln Pro Leu Met Asp $340 \hspace{1.5cm} 345 \hspace{1.5cm} 350 \hspace{1.5cm}$

Lys Asn Arg Ile Glu Glu Arg Leu Asn Leu Val Glu Ala Phe Val Glu 355 360 365

Asp Ala Glu Leu Arg Gln Thr Leu Gln Glu Asp Leu Leu Arg Arg Phe 370 380

Pro Asp Leu Asn Arg Leu Ala Lys Lys Phe Gln Arg Gln Ala Ala Asn 385 390 395 400

Leu Gln Asp Cys Tyr Arg Leu Tyr Gln Gly Ile Asn Gln Leu Pro Asn 405 415

Val Ile Gln Ala Leu Glu Lys His Glu Gly Lys His Gln Lys Leu Leu \$420\$ \$425\$

Leu Ala Val Phe Val Thr Pro Leu Thr Asp Leu Arg Ser Asp Phe Ser 435 440 445

Lys Phe Gln Glu Met Ile Glu Thr Thr Leu Asp Met Asp Gln Val Glu Page 25 450 455 460

Asn His Glu Phe Leu Val Lys Pro Ser Phe Asp Pro Asn Leu Ser Glu 465 470 475 480

Leu Arg Glu Ile Met Asn Asp Leu Glu Lys Lys Met Gln Ser Thr Leu 485 490 495

Ile Ser Ala Ala Arg Asp Leu Gly Leu Asp Pro Gly Lys Gln Ile Lys 500 505

Leu Asp Ser Ser Ala Gln Phe Gly Tyr Tyr Phe Arg Val Thr Cys Lys 515 520 525

Glu Glu Lys Val Leu Arg Asn Asn Lys Asn Phe Ser Thr Val Asp Ile 530 535 540

Gln Lys Asn Gly Val Lys Phe Thr Asn Ser Lys Leu Thr Ser Leu Asn 545 550550555555

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Ile Val Lys Glu Ile Val Asn Ile Ser Ser Gly Tyr Val Glu Pro Met 580 585 590

Gln Thr Leu Asn Asp Val Leu Ala Gln Leu Asp Ala Val Val Ser Phe 595 600 605

Ala His Val Ser Asn Gly Ala Pro Val Pro Tyr Val Arg Pro Ala Ile $610 \hspace{1.5cm} 620$

Leu Glu Lys Gly Gln Gly Arg Ile Ile Leu Lys Ala Ser Arg His Ala 625 630 635

Phe Glu Lys Asp Lys Gln Met Phe His Ile Ile Thr Gly Pro Asn Met $660 \hspace{1.5cm} 665 \hspace{1.5cm} 670 \hspace{1.5cm}$

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Ala Gln Ile Gly Cys Phe Val Pro Cys Glu Ser Ala Glu Val Ser Ile 690 695 700

Val Asp Cys Ile Leu Ala Arg Val Gly Ala Gly Asp Ser Gln Leu Lys

Page 26

Gly Val Ser Thr Phe Met Ala Glu Met Leu Glu Thr Ala Ser Ile Leu

Arg Ser Ala Thr Lys Asp Ser Leu Ile Ile Ile Asp Glu Leu Gly Arg

Gly Thr Ser Thr Tyr Asp Gly Phe Gly Leu Ala Trp Ala Ile Ser Glu 755 760

Tyr Ile Ala Thr Lys Ile Gly Ala Phe Cys Met Phe Ala Thr His Phe

His Glu Leu Thr Ala Leu Ala Asn Gln Ile Pro Thr Val Asn Asn Leu 785 790 795

His Val Thr Ala Leu Thr Thr Glu Glu Thr Leu Thr Met Leu Tyr Gln

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Leu Ala Asn Phe Pro Lys His Val Ile Glu Cys Ala Lys Gln Lys Ala

Leu Glu Leu Glu Glu Phe Gln Tyr Ile Gly Glu Ser Gln Gly Tyr Asp

Ile Met Glu Pro Ala Ala Lys Lys Cys Tyr Leu Glu Arg Glu Gln Gly

Glu Lys Ile Ile Gln Glu Phe Leu Ser Lys Val Lys Gln Met Pro Phe

Thr Glu Met Ser Glu Glu Asn Ile Thr Ile Lys Leu Lys Gln Leu Lys 900 905 910

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Ser Tyr Ser Asp Gly Lys Leu Lys Ala Pro Pro Lys Pro Cys Ala Gly 130 135

Asn Gln Gly Thr Gln Ile Thr Val Glu Asp Leu Phe Tyr Asn Ile Ala 145 \$150\$

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Leu Glu Val Val Gly Arg Tyr Ser Val His Asn Ala Gly Ile Ser Phe 180 185 190

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Leu Leu Ile Asp Asn Tyr Val Pro Pro Leu Glu Gly Leu Pro Ile Phe 645 650 655

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Asp Ala Pro Val Met Ala Met Lys Tyr Tyr Thr Ser Lys Ile Asn Ser 65 70 75 80

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Asp Ile Gly Gly Ser Asp Val Glu Phe Lys Pro Asp Thr Lys Glu Glu

Gly Ser Ser Asp Glu Ile Ser Ser Gly Val Gly Asp Ser Glu Ser Glu 275 280 285

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Asp Leu Glu Arg Leu Leu Ser Lys Ile His Asn Val Gly Ser Pro Leu 820 825 830

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Thr Tyr Ser Lys Lys Lys Ile Ile Asp Phe Leu Ser Ala Leu Glu Gly 850 860

Phe Lys Val Met Cys Lys Ile Ile Gly Ile Met Glu Glu Val Ala Asp 865 870 875

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Thr Leu Leu Leu Ala Phe Gly Lys Asn Ala Val Arg Cys Ala Leu Ile 65 70 75 80

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Gly Glu Lys Glu Arg Arg Glu Val Phe Phe Pro Pro Arg Pro Glu Arg

Val Glu His Asn Val Glu Ser Ser Arg Trp Glu Pro Arg Arg Gly

Ala Cys Gly Ser Arg Gly Gly Asn Phe Pro Ser Pro Arg Gly Gly Ser 130 135 140

Gly Val Ala Ser Leu Glu Arg Ala Glu Asn Ser Ser Thr Glu Pro Ala 145 150 155 160

Lys Ala Ile Lys Pro Ile Asp Arg Lys Ser Val His Gln Ile Cys Ser Page 42

175 *

Gly Pro Val Val Pro Ser Leu Arg Pro Asn Ala Val Lys Glu Leu Val

Glu Asn Ser Leu Asp Ala Gly Ala Thr Asn Val Asp Leu Lys Leu Lys

Asp Tyr Gly Val Asp Leu Ile Glu Val Ser Gly Asn Gly Cys Gly Val

Glu Glu Glu Asn Phe Glu Gly Phe Thr Leu Lys His His Thr Cys Lys 230 235

Ile Gln Glu Phe Ala Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg 245

Gly Glu Ala Leu Ser Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser 260

Thr Cys Arg Val Ser Ala Lys Val Gly Thr Arg Leu Val Phe Asp His 275

Tyr Gly Lys Ile Ile Gln Lys Thr Pro Tyr Pro Arg Pro Arg Gly Met

Thr Val Ser Val Lys Gln Leu Phe Ser Thr Leu Pro Val His His Lys 315 305 310

Glu Phe Gln Arg Asn Ile Lys Lys Lys Arg Ala Cys Phe Pro Phe Ala

Phe Cys Arg Asp Cys Gln Phe Pro Glu Ala Ser Pro Ala Met Leu Pro

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Asp Arg Arg Gly Pro Arg Glu Gln Thr Arg Ala Pro Ala Thr Ala Ala 50 55 60

Pro Pro Arg Pro Leu Gly Ser Arg Gly Ala Glu Ala Ala Glu Pro Gln 65 70 70 75 80

Glu Gly Leu Ser Ala Thr Val Ser Ala Cys Phe Gln Glu Gln Glu 85 90 95

Met Asn Thr Leu Gln Gly Pro Val Ser Phe Lys Asp Val Ala Val Asp

Phe Thr Gln Glu Glu Trp Arg Gln Leu Asp Pro Asp Glu Lys Ile Ala 115 120 125

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Tyr Asp Tyr His Gln Ala Lys His His His Gly Val Glu Val Lys Glu 145 150 155 160

Val Glu Gln Gly Glu Pro Trp Ile Met Glu Gly Glu Phe Pro Cys 165 170 175

Gln His Ser Pro Glu Pro Ala Lys Ala Ile Lys Pro Ile Asp Arg Lys 180 185 190

Ser Val His Gln Ile Cys Ser Gly Pro Val Val Leu Ser Leu Ser Thr 195 200 205

Ala Val Lys Glu Leu Val Glu Asn Ser Leu Asp Ala Gly Ala Thr Asn 210 215220

Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp Leu Ile Glu Val Ser 225 230230235

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Pro Pro Arg Pro Leu Gly Ser Arg Gly Ala Glu Ala Ala Glu Pro Gln 65 70 75 80

Glu Gly Leu Ser Ala Thr Val Ser Ala Cys Phe Gln Glu Gln Gln Glu 85 90 95

Met Asn Thr Leu Gln Gly Pro Val Ser Phe Lys Asp Val Ala Val Asp $100 \hspace{1.5cm} 100 \hspace{1.5cm} 105 \hspace{1.5cm} 110 \hspace{1.5cm}$

Phe Thr Gln Glu Glu Trp Arg Gln Leu Asp Pro Asp Glu Lys Ile Ala 115 120 125

Tyr Gly Asp Val Met Leu Glu Asn Tyr Ser His Leu Val Ser Val Gly 130 135 140

Tyr Asp Tyr His Gln Ala Lys His His Gly Val Glu Val Lys Glu 145 \$150\$

Val Glu Gln Gly Glu Glu Pro Trp Ile Met Glu Gly Glu Phe Pro Cys 165 170 175

Gln His Ser Pro Glu Pro Ala Lys Ala Ile Lys Pro Ile Asp Arg Lys 180 185 190

Ser Val His Gln Ile Cys Ser Gly Pro Val Val Leu Ser Leu Ser Thr 195 200 205

Ala Val Lys Glu Leu Val Glu Asn Ser Leu Asp Ala Gly Ala Thr Asn 210 215 220

Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp Leu Ile Glu Val Ser 225 230 235 240

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rget mismatch repair gene

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4290

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Thr Phe Gln Val Gln Val Ile Asp Asn Gly Phe Gly Met Gly Ser Asp 50 55 60

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Val Gln Asp Leu Glu Asn Pro Arg Phe Tyr Gly Phe Arg Gly Glu Ala 85 90 95

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Lys Asn Arg Thr Met Lys Thr Phe Val Lys Leu Phe Gln Ser Gly Lys 115 \$120\$

Ala Leu Lys Ala Cys Glu Ala Asp Val Thr Arg Ala Ser Ala Gly Thr 130 140

Thr Val Thr Val Tyr Asn Leu Phe Tyr Gln Leu Pro Val Arg Arg Lys 145 $$ 150 $$ 155 $$ 160

Cys Met Asp Pro Arg Leu Glu Phe Glu Lys Val Arg Gln Arg Ile Glu 165 170 175

Ala Leu Ser Leu Met His Pro Ser Ile Ser Phe Ser Leu Arg Asn Asp 180 185 190

Val Ser Gly Ser Met Val Leu Gln Leu Pro Lys Thr Lys Asp Val Cys 195 200 205

Ser Arg Phe Cys Gln Ile Tyr Gly Leu Gly Lys Ser Gln Lys Leu Arg 210 215 220

Glu Ile Ser Phe Lys Tyr Lys Glu Phe Glu Leu Ser Gly Tyr Ile Ser 225 230 235 240

Ser Glu Ala His Tyr Asn Lys Asn Met Gln Phe Leu Phe Val Asn Lys

Arg Leu Val Leu Arg Thr Lys Leu His Lys Leu Ile Asp Phe Leu Leu

Arg Lys Glu Ser Ile Ile Cys Lys Pro Lys Asn Gly Pro Thr Ser Arg

Gln Met Asn Ser Ser Leu Arg His Arg Ser Thr Pro Glu Leu Tyr Gly 290 300

Ile Tyr Val Ile Asn Val Gln Cys Gln Phe Cys Glu Tyr Asp Val Cys 305 310 315 320

Met Glu Pro Ala Lys Thr Leu Ile Glu Phe Gln Asn Trp Asp Thr Leu 325 $$ 330 $$ 335

Leu Phe Cys Ile Gln Glu Gly Val Lys Met Phe Leu Lys Gln Glu Lys 340 345

Leu Phe Val Glu Leu Ser Gly Glu Asp Ile Lys Glu Phe Ser Glu Asp 355 360 365

Asn Gly Phe Ser Leu Phe Asp Ala Thr Leu Gln Lys Arg Val Thr Ser 370 380

Asp Glu Arg Ser Asn Phe Gln Glu Ala Cys Asn Asn Ile Leu Asp Ser 385 $$ 390 $$ 395 $$ 400

Tyr Glu Met Phe Asn Leu Gln Ser Lys Ala Val Lys Arg Lys Thr Thr $405 \hspace{1cm} 410 \hspace{1cm} 415$

Ala Glu'Asn Val Asn Thr Gln Ser Ser Arg Asp Ser Glu Ala Thr Arg 420 425 430

Gly His Ser Lys Met Thr Glu Pro Ser Leu Gln Asn Lys Asp Ser Ser 450 460

Cys Ser Glu Ser Lys Met Leu Glu Glu Glu Thr Ile Val Ala Ser Glu 465 470470475475

Ala Gly Glu Asn Glu Lys His Lys Lys Ser Phe Leu Glu His Ser Ser 485 490 495

Leu Glu Asn Pro Cys Gly Thr Ser Leu Glu Met Phe Leu Ser Pro Phe 500 505 510

Gln Thr Pro Cys His Phe Glu Glu Ser Gly Gln Asp Leu Glu Ile Trp 515 520 525

- Lys Glu Ser Thr Thr Val Asn Gly Met Ala Ala Asn Ile Leu Lys Asn 530 535
- Asn Arg Ile Gln Asn Gln Pro Lys Arg Phe Lys Asp Ala Thr Glu Val 545 550 555
- Gly Cys Gln Pro Leu Pro Phe Ala Thr Thr Leu Trp Gly Val His Ser 565 570 575
- Ala Gln Thr Glu Lys Glu Lys Lys Glu Ser Ser Asn Cys Gly Arg
 580 585 590
- Arg Asn Val Phe Ser Tyr Gly Arg Val Lys Leu Cys Ser Thr Gly Phe $595 \hspace{1cm} 600 \hspace{1cm} 605$
- Ile Thr His Val Val Gln Asn Glu Lys Thr Lys Ser Thr Glu Thr Glu
- His Ser Phe Lys Asn Tyr Val Arg Pro Gly Pro Thr Arg Ala Glu G25 $_{\rm 630}$
- Thr Phe Gly Asn Arg Thr Arg His Ser Val Glu Thr Pro Asp Ile Lys 645 650 655
- Asp Leu Ala Ser Thr Leu Ser Lys Glu Ser Gly Gln Leu Pro Asn Lys 660665665
- Lys Asn Cys Arg Thr Asn Ile Ser Tyr Gly Leu Glu Asn Glu Pro Thr
- Ala Thr Tyr Thr Met Phe Ser Ala Phe Gln Glu Gly Ser Lys Lys Ser 690 $\,$ 700 $\,$
- Gln Thr Asp Cys Ile Leu Ser Asp Thr Ser Pro Ser Phe Pro Trp Tyr 705 $$ 710 $$ 710 $$ 720
- Arg His Val Ser Asn Asp Ser Arg Lys Thr Asp Lys Leu Ile Gly Phe $725 \hspace{1cm} 730 \hspace{1cm} 735$
- Ser Lys Pro Ile Val Arg Lys Lys Leu Ser Leu Ser Ser Gln Leu Gly 740
- Ser Leu Glu Lys Phe Lys Arg Gln Tyr Gly Lys Val Glu Asn Pro Leu
- Asp Thr Glu Val Glu Glu Ser Asn Gly Val Thr Thr Asn Leu Ser Leu 770 775 780

Gln Val Glu Pro Asp Ile Leu Leu Lys Asp Lys Asn Arg Leu Glu Asn 785 790 795 800

Ser Asp Val Cys Lys Ile Thr Thr Met Glu His Ser Asp Ser Asp Ser 805 810 815

Ser Cys Gln Pro Ala Ser His Ile Leu Asp Ser Glu Lys Phe Pro Phe 820 825 830

Ser Lys Asp Glu Asp Cys Leu Glu Gln Gln Met Leu Ser Leu Arg Glu 835 840 845

Ser Pro Met Thr Leu Lys Glu Leu Ser Leu Phe Asn Arg Lys Pro Leu 850 850 860

Asp Leu Glu Lys Ser Ser Glu Ser Leu Ala Ser Lys Leu Ser Arg Leu 865 870 875 880

Lys Gly Ser Glu Arg Glu Thr Gln Thr Met Gly Met Met Ser Arg Phe 885 890 895

Asn Glu Leu Pro Asn Ser Asp Ser Ser Arg Lys Asp Ser Lys Leu Cys 900 905 910

Ser Val Leu Thr Gln Asp Phe Cys Met Leu Phe Asn Asn Lys His Glu 915 920 925

Lys Thr Glu Asn Gly Val Ile Pro Thr Ser Asp Ser Ala Thr Gln Asp $930 \\ 935 \\ 940$

Asn Ser Phe Asn Lys Asn Ser Lys Thr His Ser Asn Ser Asn Thr Thr 945 950 950

Glu Asn Cys Val Ile Ser Glu Thr Pro Leu Val Leu Pro Tyr Asn Asn 965 970 975

Ser Lys Val Thr Gly Lys Asp Ser Asp Val Leu Ile Arg Ala Ser Glu 980 985 990

Gln Gln Ile Gly Ser Leu Asp Ser Pro Ser Gly Met Leu Met Asn Pro 995 $1000\,$

Val Glu Asp Ala Thr Gly Asp Gln Asn Gly Ile Cys Phe Gln Ser 1010 1015 1020

Glu Glu Ser Lys Ala Arg Ala Cys Ser Glu Thr Glu Glu Ser Asn 1025 1030 1035 Thr Cys Cys Ser Asp Trp Gln Arg His Phe Asp Val Ala Leu Gly

Arg Met Val Tyr Val Asn Lys Met Thr Gly Leu Ser Thr Phe Ile 1055 1060 1065

Ala Pro Thr Glu Asp Ile Gln Ala Ala Cys Thr Lys Asp Leu Thr

Thr Val Ala Val Asp Val Val Leu Glu Asn Gly Ser Gln Tyr Arg 1085 1090 1095

Cys Gln Pro Phe Arg Ser Asp Leu Val Leu Pro Phe Leu Pro Arg

Ala Arg Ala Glu Arg Thr Val Met Arg Gln Asp Asn Arg Asp Thr 1115 $$ 1120 $$ 1125

Val Asp Asp Thr Val Ser Ser Glu Ser Leu Gln Ser Leu Phe Ser 1130

Glu Trp Asp Asn Pro Val Phe Ala Arg Tyr Pro Glu Val Ala Val 1145 1150 1155

Asp Val Ser Ser Gly Gln Ala Glu Ser Leu Ala Val Lys Ile His 1160 \$1160\$

Asn Ile Leu Tyr Pro Tyr Arg Phe Thr Lys Gly Met Ile His Ser 1175 1180 1185

Met Gln Val Leu Gln Gln Val Asp Asn Lys Phe Ile Ala Cys Leu 1190 1195 1200

Met Ser Thr Lys Thr Glu Glu Asn Gly Glu Ala Asp Ser Tyr Glu 1205 1210 1215

Lys Gln Gln Ala Gln Gly Ser Gly Arg Lys Lys Leu Leu Ser Ser 1220 1225 1230

Thr Leu Ile Pro Pro Leu Glu Ile Thr Val Thr Glu Glu Gln Arg

Arg Leu Leu Trp Cys Tyr His Lys Asn Leu Glu Asp Leu Gly Leu 1250 1255 1260

Glu Phe Val Phe Pro Asp Thr Ser Asp Ser Leu Val Leu Val Gly 1265 1270 1275

	1280					1285					1290			
Arg	Gly 1295	Arg	Ser	Thr	Val	Thr 1300	Lys	Ser	Ile	Val	Glu 1305	Glu	Phe	Ile
Arg	Glu 1310		Leu	Glu	Leu	Leu 1315	Gln	Thr	Thr	Gly	Gly 1320	Ile	Gln	Gly
Thr	Leu 1325		Leu	Thr	Val	Gln 1330		Val	Leu	Ala	Ser 1335	Gln	Ala	Cys
His	Gly 1340		Ile	Lys		Asn 1345	Asp	Gly	Leu	Ser	Leu 1350	Gln	Glu	Ser
Cys	Arg 1355		Ile	Glu		Leu 1360		Ser	Cys	Gln	Leu 1365	Pro	Phe	Gln
Cys	Ala 1370		Gly	Arg	Pro	Ser 1375	Met	Leu	Pro	Leu	Ala 1380	Asp	Ile	Asp
His	Leu 1385		Gln	Glu	Lys	Gln 1390	Ile	Lys	Pro	Asn	Leu 1395	Thr	Lys	Leu
Arg	Lys 1400	Met	Ala	Gln	Ala	Trp 1405	Arg	Leu	Phe	Gly	Lys 1410	Ala	Glu	Cys
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Pro														
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gteaaggage tigtegagaa tagtetegae geeggegeea eeagtataga gattaacete 180
egagactaeg gegaagacta titteaggie attgacaatg gittgiggeat titeeceaace 240
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Leu Asp Ala Gly Ala Thr Ser Ile Glu Ile Asn Leu Arg Asp Tyr Gly

Glu Asp Tyr Phe Gln Val Ile Asp Asn Gly Cys Gly Ile Ser Pro Thr

Asn Phe Lys Val Cys Val Gln Ile Leu Arg Arg Thr Phe Asp Val Leu

Ala Leu Lys His His Thr Ser Lys Leu Glu Asp Phe Thr Asp Leu Leu 100

Asn Leu Thr Thr Tyr Gly Phe Arg Gly Glu Ala Leu Ser Ser Leu Cys

Ala Leu Gly Asn Leu Thr Val Glu Thr Arg Thr Lys Asn Glu Pro Val 130 135 140

Ala Thr Leu Leu Thr Phe Asp His Ser Gly Leu Leu Thr Ala Glu Lys 150

Lys Thr Ala Arg Gln Ile Gly Thr Thr Val Thr Val Arg Lys Leu Phe 165 170

Ser Asn Leu Pro Val Arg Ser Lys Glu Phe Lys Arg Asn Ile Arg Lys

Glu Tyr Gly Lys Leu Val Ser Leu Leu Asn Ala Tyr Ala Leu Ile Ala 195 200

Lys Gly Val Arg Phe Val Cys Ser Asn Thr Thr Gly Lys Asn Pro Lys 210

Ser Val Val Teu Asn Thr Gln Gly Arg Gly Ser Leu Lys Asp Asn Ile 225 230 235 240

Ile Thr Val Phe Gly Ile Ser Thr Phe Thr Ser Leu Gln Pro Gly Thr 245 250 255

Gly Arg Asn Leu Ala Asp Arg Gln Tyr Phe Phe Ile Asn Gly Arg Pro $260 \\ 260 \\ 265 \\ 270 \\ 270$

Val Asp Met Pro Lys Val Ser Lys Leu Val Asn Glu Leu Tyr Lys Asp 275 280 285

Thr Ser Ser Arg Lys Tyr Pro Val Thr Ile Leu Asp Phe Ile Val Pro 290 295 300

Gly Gly Ala Cys Asp Leu Asn Val Thr Pro Asp Lys Arg Lys Val Phe 305 310 315

Phe Ser Asp Glu Thr Ser Val Ile Gly Ser Leu Arg Glu Gly Leu Asn 325 330 335

Glu Ile Tyr Ser Ser Ser Asn Ala Ser Tyr Ile Val Asn Arg Phe Glu $_{340}$

Glu Asn Ser Glu Gln Pro Asp Lys Ala Gly Val Ser Ser Phe Gln Lys 355 360 365

Lys Ser Asn Leu Leu Ser Glu Gly Ile Val Leu Asp Val Ser Ser Lys $370 \hspace{1.5cm} 375 \hspace{1.5cm} 380 \hspace{1.5cm}$

Thr Arg Leu Gly Glu Ala Ile Glu Lys Glu Asn Pro Ser Leu Arg Glu 385 390 395 400

Val Glu Ile Asp Asn Ser Ser Pro Met Glu Lys Phe Lys Phe Glu Ile 405 410 415

Lys Ala Cys Gly Thr Lys Lys Gly Glu Gly Ser Leu Ser Val His Asp $420 \hspace{1.5cm} 425 \hspace{1.5cm} 430 \hspace{1.5cm}$

Val Thr His Leu Asp Lys Thr Pro Ser Lys Gly Leu Pro Gln Leu Asn 435 440 445

Val Thr Glu Lys Val Thr Asp Ala Ser Lys Asp Leu Ser Ser Arg Ser 450 455 460

Ser Phe Ala Gln Ser Thr Leu Asn Thr Phe Val Thr Met Gly Lys Arg 465 470 475 480

Page 61

- Lys His Glu Asn Ile Scr Thr Ile Leu Ser Glu Thr Pro Val Leu Arg 485 490 495
- Asn Gln Thr Ser Ser Tyr Arg Val Glu Lys Ser Lys Phe Glu Val Arg 500
- Ala Leu Ala Ser Arg Cys Leu Val Glu Gly Asp Gln Leu Asp Asp Met 515 520 525
- Val Ile Ser Lys Glu Asp Met Thr Pro Ser Glu Asp Asp Ser Glu Leu 530 535 540
- Gly Asn Arg Ile Ser Pro Gly Thr Gln Ala Asp Asn Val Glu Arg His 545 550 555 560
- Glu Arg Val Leu Gly Gln Phe Asn Leu Gly Phe Ile Ile Ala Lys Leu 565 570 575
- Glu Arg Asp Leu Phe Ile Val Asp Gln His Ala Ala Asp Glu Lys Phe 580 585 590
- Asn Phe Glu His Leu Ala Arg Ser Thr Val Leu Asn Gln Gln Pro Leu 595 600 605
- Leu Gln Pro Leu Asn Leu Glu Leu Ser Pro Glu Glu Glu Val Thr Val 610 610
- Leu Met His Met Asp Ile Ile Arg Glu Asn Gly Phe Leu Leu Glu Glu 625 630 635
- Asn Pro Ser Ala Pro Pro Gly Lys His Phe Arg Leu Arg Ala Ile Pro $_{645}$ $_{650}$ $_{650}$
- Tyr Ser Lys Asn Ile Thr Phe Gly Val Glu Asp Leu Lys Asp Leu Ile 660 665 670
- Ser Thr Leu Gly Asp Asn His Gly Glu Cys Ser Val Ala Ser Ser Tyr 675 680 685
- Lys Thr Ser Lys Thr Asp Ser Ile Cys Pro Ser Arg Val Arg Ala Met
- Leu Ala Ser Arg Ala Cys Arg Ser Ser Val Met Ile Gly Asp Pro Leu 705 710 715 720
- Arg Lys Asn Glu Met Gln Lys Ile Val Glu His Leu Ala Asp Leu Glu
 725 730 735

Ser Pro Trp Asn Cys Pro His Gly arg Pro Thr Met Arg His Leu Val

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1320

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3300

3360

3420

3456

Lys Tyr Met Gln Ser Ser Pro Lys Lys Val Leu Glu Ser Ile Lys Lys 165 170 175

Cys Val Phe Arg Ile Ala Leu Val His Ser Asn Val Ser Phe Ser Val

Leu Asp Ile Glu Ser Asp Glu Glu Leu Phe Gln Thr Asn Pro Ser Sex

Ser Ala Phe Ser Leu Leu Met Arg Asp Ala Gly Thr Glu Ala Val Asn 210 $$ 215 $$ 220

Ser Leu Cys Lys Val Asn Val Thr Asp Gly Met Leu Asn Val Ser Gly 225 235 240

Phe Glu Cys Ala Asp Asp Trp Lys Pro Thr Asp Gly Gln Gln Thr Gly 245 250 255

Arg Arg Asn Arg Leu Gln Ser Asn Pro Gly Tyr Ile Leu Cys Ile Ala $260 \hspace{1.5cm} 265 \hspace{1.5cm} 270 \hspace{1.5cm}$

Cys Pro Arg Arg Leu Tyr Glu Phe Ser Phe Glu Pro Ser Lys Thr His

Val Glu Phe Lys Lys Trp Gly Pro Val Leu Ala Phe Ile Glu Arg Ile 290 295 300

Thr Leu Ala Asn Trp Lys Lys Asp Arg Ile Leu Glu Leu Phe Asp Gly 305 310 315 320

Gly Ala Asp Ile Leu Ala Lys Gly Asp Arg Gln Asp Leu Ile Asp Asp 325 330 335

Lys Ile Arg Leu Gln Asn Gly Ser Leu Phe Ser Ile Leu His Phe Leu 340 345 350

Asp Ala Asp Trp Pro Glu Ala Met Glu Pro Ala Lys Lys Lys Leu Lys 355 360 365

Arg Ser Asn Asp His Ala Pro Cys Ser Ser Leu Leu Phe Pro Ser Ala 370 375 380

Asp Phe Lys Gln Asp Gly Asp Tyr Phe Ser Pro Arg Lys Asp Val Trp 385 390 395 400

Ser Pro Glu Cys Glu Val Glu Leu Lys Ile Gln Asn Pro Lys Glu Gln 405 410 415

Gly Thr Val Ala Gly Phe Glu Ser Arg Thr Asp Ser Leu Leu Gln Ser 420 425 430

Arg Asp Ile Glu Met Gln Thr Asn Glu Asp Phe Pro Gln Val Thr Asp $435 \hspace{1.5cm} 440 \hspace{1.5cm} 445$

Leu Leu Glu Thr Ser Leu Val Ala Asp Ser Lys Cys Arg Lys Gln Phé 450 460

Leu Thr Arg Cys Gln Ile Thr Thr Pro Val Asn Ile Asn His Asp Phe 465 470 475 480

Met Lys Asp Ser Asp Val Leu Asn Phe Gln Phe Gln Gly Leu Lys Asp 485 490 495

Glu Leu Asp Val Ser Asn Cys Ile Gly Lys His Leu Leu Arg Gly Cys
500 505 510

Ser Ser Arg Val Ser Leu Thr Phe His Glu Pro Lys Leu Ser His Val

Glu Gly Tyr Glu Ser Val Val Pro Met Ile Pro Asn Glu Lys Gln Ser 530 540

Ser Pro Arg Val Leu Glu Thr Arg Glu Gly Gly Ser Tyr Cys Asp Val 545 550 555 560

Tyr Ser Asp Lys Thr Pro Asp Cys Ser Leu Gly Ser Ser Trp Gln Asp 565 575

Thr Asp Trp Phe Thr Pro Gln Cys Ser Ser Asp Arg Gly Cys Val Gly $_{580}$

Ile Gly Glu Asp Phe Asn Ile Thr Pro Ile Asp Thr Ala Glu Phe Asp 595 600

Ser Tyr Asp Glu Lys Val Gly Ser Lys Lys Tyr Leu Ser Ser Val Asn 610 615 620

Val Gly Ser Ser Val Thr Gly Ser Phe Cys Leu Ser Ser Glu Trp Ser 625 $$ 630 $$ 630 $$ 640

Pro Met Tyr Ser Thr Pro Ser Ala Thr Lys Trp Glu Ser Glu Tyr Gln 645 650 655

Lys Gly Cys Arg Ile Leu Glu Gln Ser Leu Arg Leu Gly Arg Met Pro 660 665 670

Asp Pro Glu Phe Cys Phe Ser Ala Ala Asn Asn Ile Lys Phe Asp His 675 680 685

Glu Val Ile Pro Glu Met Asp Cys Cys Glu Thr Gly Thr Asp Ser Phe 690 695 700

Thr Ala Ile Gln Asn Cys Thr Gln Leu Ala Asp Lys Ile Cys Lys Ser 715 Ser Trp Gly His Ala Asp Asp Val Arg Ile Asp Gln Tyr Ser Ile Arg 725 735

Lys Glu Lys Phe Ser Tyr Met Asp Gly Thr Gln Asn Asn Ala Gly Lys $740 \hspace{1cm} 745 \hspace{1cm} 750 \hspace{1cm} 750 \hspace{1cm}$

Gln Arg Ser Lys Arg Ser Arg Ser Ala Pro Pro Phe Tyr Arg Glu Lys 755 760 765

Lys Arg Phe Ile Ser Leu Ser Cys Lys Ser Asp Thr Lys Pro Lys Asn 770 775 780

Ser Asp Pro Ser Glu Pro Asp Asp Leu Glu Cys Leu Thr Gln Pro Cys 785 790 795 800

Asn Ala Ser Gln Met His Leu Lys Cys Ser Ile Leu Asp Asp Val Ser 805 810 810

Tyr Asp His Ile Gln Glu Thr Glu Lys Arg Leu Ser Ser Ala Ser Asp 825 $\,$ 830 $\,$

Leu Lys Ala Ser Ala Gly Cys Arg Thr Val His Ser Glu Thr Gln Asp 835 840

Glu Asp Val His Glu Asp Phe Ser Ser Glu Glu Phe Leu Asp Pro Ile 850 855 860

Lys Ser Thr Thr Lys Trp Arg His Asn Cys Ala Val Ser Gln Val Pro 865 870 875

Lys Glu Ser His Glu Leu His Gly Gln Asp Gly Val Phe Asp Ile Ser 885 890 895

Ser Gly Leu Leu His Leu Arg Ser Asp Glu Ser Leu Val Pro Glu Ser

Ile Asn Arg His Ser Leu Glu Asp Ala Lys Val Leu Gln Gln Val Asp 915 920 925

Lys Lys Tyr Ile Pro Ile Val Ala Cys Gly Thr Val Ala Ile Val Asp 930 935 940

Gln His Ala Ala Asp Glu Arg Ile Arg Leu Glu Glu Leu Arg Thr Lys 945 950 950 955

Phe	Ile	Asn		Ala 1 965	Leu I	Leu I	le Ph	ie Va 97	l Le O	u Th	r Leu	Lys	Val 975	Leu
Pro	Glu	Met	Gly 980	Tyr	31n 1	Leu L	eu Gl 98	n Se	т Ту	r Se	er Glu	Gln 990	Ile	Arg
Asp	Trp	Gly 995	Trp	Ile	Cys i	Asn I	le 1	hr V	al G	lu G	ly Se	r T 05	hr S	er Phe
Lys	Lys 1010	Asr	Met	Ser	Ile	Ile 1015	Gln	Arg	Lys	Pro	Thr 1020	Pro	Ile	Thr
Leu	Asn 1025		val	Pro	Cys	Ile 1030	Leu	Gly	Val	Asn	Leu 1035	Ser	Asp	Val
Asp	Leu 1040		ı Glu	ı Phe	Leu	Gln 1045	Gln	Leu	Ala	Asp	Thr 1050	Asp	Gly	Ser
Ser	Thr 105		e Pro	Pro	Ser	Val 1060	Leu	Arg	Val	Leu	Asn 1065	Ser	Lys	Ala
Cys	Arg		y Ala	a Ile	Met	Phe 1075	Gly	Asp	Ser	Leu	Leu 1080	Pro	Ser	Glu
Cys	Ser		u Ile	e Ile	Asp	Gly 1090		Lys	Gln	Thr	Ser 1095	Leu	Сув	Phe
Gln	Cys 110		a Hi	s Gly	Arg	Pro 1109	Thr	Thr	Val	Pro	Leu 1110	Val	Asp	Leu
Lys	Ala 111		u Hi	s Lys	Glr	Ile 1120	Ala	Lys	Leu	Ser	Gly 1125	Arg	Gln	Val
Trp	His 113	G1 0	y Le	u Glr	n Arg	113	Glu 5	Ile	Thr	Leu	Asp 1140	Arg	Ala	Lys
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ggt	ttgg													atttaat
			~~~				agat	toto	+ 200	++ +	tacta	tttc	gaa	atctqtc

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Asp Ala Ser Val Arg Phe Ala Val Ser Lys Ser Val Asp Glu Val Arg 50 60

Gly Inr Asp Thr Pro Pro Glu Lys Val Pro Arg Arg Val Leu Pro Ser 65 70 80

Gly Phe Lys Pro Ala Glu Ser Ala Gly Asp Ala Ser Ser Leu Phe Ser 85 90 95

Glu Arg Ser Arg Glu Asp Val Val Pro Leu Asn Asp Ser Ser Leu Cys 115 120 125

Met Lys Ala Asn Asp Val Ile Pro Gln Phe Arg Ser Asn Asn Gly Lys 130 135 140

Thr Gln Glu Arg Asn His Ala Phe Ser Phe Ser Gly Arg Ala Glu Leu 145 \$150\$

Arg Ser Val Glu Asp Ile Gly Val Asp Gly Asp Val Pro Gly Pro Glu 165 170 175

Thr Pro Gly Met Arg Pro Arg Ala Ser Arg Leu Lys Arg Val Leu Glu 180 185 190

Asp Glu Met Thr Phe Lys Glu Asp Lys Val Pro Val Leu Asp Ser Asn  $195 \hspace{1cm} 200 \hspace{1cm} 200 \hspace{1cm} 205 \hspace{1cm}$ 

Lys Arg Leu Lys Met Leu Gln Asp Pro Val Cys Gly Glu Lys Lys Glu 210  $\,$  215  $\,$  220  $\,$ 

Val Asn Glu Gly Thr Lys Phe Glu Trp Leu Glu Ser Ser Arg Ile Arg 225 230 235

Asp Ala Asn Arg Arg Arg Pro Asp Asp Pro Leu Tyr Asp Arg Lys Thr 245  $\phantom{0}250$ 

Leu His Ile Pro Pro Asp Val Phe Lys Lys Met Ser Ala Ser Gln Lys 260 265

Gln Tyr Trp Ser Val Lys Ser Glu Tyr Met Asp Ile Val Leu Phe Phe 275 280 285

Lys Val Gly Lys Phe Tyr Glu Leu Tyr Glu Leu Asp Ala Glu Leu Gly

His Lys Glu Leu Asp Trp Lys Met Thr Met Ser Gly Val Gly Lys Cys

Arg Gln Val G! Ile Ser Glu Ser Gly Ile Asp Glu Ala Val Gln Lys 325 Leu Leu Ala Arg Gly Tyr Lys Val Gly Arg Ile Glu Gln Leu Glu Thr Ser Asp Gln Ala Lys Ala Arg Gly Ala Asn Thr Ile Ile Pro Arg Lys 360 Leu Val Gln Val Leu Thr Pro Ser Thr Ala Ser Glu Gly Asn Ile Gly Pro Asp Ala Val His Leu Leu Ala Ile Lys Glu Ile Lys Met Glu Leu Gln Lys Cys Ser Thr Val Tyr Gly Phe Ala Phe Val Asp Cys Ala Ala Leu Arg Phe Trp Val Gly Ser Ile Ser Asp Asp Ala Ser Cys Ala Ala Leu Gly Ala Leu Leu Met Gln Val Ser Pro Lys Glu Val Leu Tyr Asp 435 Ser Lys Gly Leu Ser Arg Glu Ala Gln Lys Ala Leu Arg Lys Tyr Thr 455 450 Leu Thr Gly Ser Thr Ala Val Gln Leu Ala Pro Val Pro Gln Val Met 465 Gly Asp Thr Asp Ala Ala Gly Val Arg Asn Ile Ile Glu Ser Asn Gly Tyr Phe Lys Gly Ser Ser Glu Ser Trp Asn Cys Ala Val Asp Gly Leu Asn Glu Cys Asp Val Ala Leu Ser Ala Leu Gly Glu Leu Ile Asn His Leu Ser Arg Leu Lys Leu Glu Asp Val Leu Lys His Gly Asp Ile Phe Pro Tyr Gln Val Tyr Arg Gly Cys Leu Arg Ile Asp Gly Gln Thr Met 545 550 Val Asn Leu Glu Ile Phe Asn Asn Ser Cys Asp Gly Gly Pro Ser Gly 565 570

Thr Leu Tyr Lys Tyr Leu .sp Asn Cys Val Ser Pro Thr Gly Lys Arg 580 585

Leu Leu Arg Asn Trp Ile Cys His Pro Leu Lys Asp Val Glu Ser Ile 595 600 605

Asn Lys Arg Leu Asp Val Val Glu Glu Phe Thr Ala Asn Ser Glu Ser 610 620

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Gly Gln Ile Val Lys Gly Phe Arg Ser Gly Ile Asp Leu Leu Ala 675 680 685

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Leu Pro Ile Leu Val Gly Lys Ser Gly Leu Glu Leu Phe Leu Ser Gln 705 710 720

Phe Glu Ala Ala Ile Asp Ser Asp Phe Pro Asn Tyr Gln Asn Gln Asp 725 730 735

Val Thr Asp Glu Asn Ala Glu Thr Leu Thr Ile Leu Ile Glu Leu Phe 740  $\phantom{000}745$   $\phantom{000}750$ 

Ile Glu Arg Ala Thr Gln Trp Ser Glu Val Ile His Thr Ile Ser Cys 755 760 765

Leu Asp Val Leu Arg Ser Phe Ala Ile Ala Ala Ser Leu Ser Ala Gly 770 780

Ser Met Ala Arg Pro Val Ile Phe Pro Glu Ser Glu Ala Thr Asp Gln 785 790 795 800

Asn Gln Lys Thr Lys Gly Pro Ile Leu Lys Ile Gln Gly Leu Trp His

Pro Phe Ala Val Ala Ala Asp Gly Gln Leu Pro Val Pro Asn Asp Ile 820 825 830 Leu Leu Gly Glu Ala Arg Arg Ser Sc  $^{\circ}$  Gly Ser Ile His Pro Arg Ser 835 840 845

Leu Leu Thr Gly Pro Asn Met Gly Gly Lys Ser Thr Leu Leu Arg 850 855 860

Ala Thr Cys Leu Ala Val Ile Phe Ala Gln Leu Gly Cys Tyr Val Pro 865 \$870

Gly Ala Ser Asp Arg Ile Met Thr Gly Glu Ser Thr Phe Leu Val Glu 900 905 910

Cys Thr Glu Thr Ala Ser Val Leu Gln Asn Ala Thr Gln Asp Ser Leu 915 920 925

Val Ile Leu Asp Glu Leu Gly Arg Gly Thr Ser Thr Phe Asp Gly Tyr 930 935 940

Ala Ile Ala Tyr Ser Val Phe Arg His Leu Val Glu Lys Val Gln Cys 945  $\phantom{\bigg|}$  950  $\phantom{\bigg|}$  955  $\phantom{\bigg|}$  960

Arg Met Leu Phe Ala Thr His Tyr His Pro Leu Thr Lys Glu Phe Ala 965 970 975

Ser His Pro Arg Val Thr Ser Lys His Met Ala Cys Ala Phe Lys Ser 980 985 990

Arg Ser Asp Tyr Gln Pro Arg Gly Cys Asp Gln Asp Leu Val Phe Leu 995 1000 1005

Tyr Arg Leu Thr Glu Gly Ala Cys Pro Glu Ser Tyr Gly Leu Gln 1010 · 1015 1020

Val Ala Leu Met Ala Gly Ile Pro Asn Gln Val Val Glu Thr Ala 1025  $$1030\$ 

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Trp Leu Lys Ser Leu Val Gly Ile Ser Arg Val Ala His Asn Asn 1070 1075 1080

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Leu Gly Asn Arg Gln Thr Pro Thr Leu Gly Asn Arg Gln Thr Pro Arg 35 40 45

Leu Gly Ile His Ala Arg Pro Arg Arg Arg Ala Thr Thr Ser Leu Leu 50 60

Thr Leu Leu Leu Ala Phe Gly Lys Asn Ala Val Arg Cys Ala Leu Ile 65 70 75 80

Gly Pro Gly Ser Leu Thr Ser Arg Thr Arg Pro Leu Thr Glu Pro Leu 85 90 95

Gly Glu Lys Glu Arg Arg Glu Val Phe Phe Pro Pro Arg Pro Glu Arg

Val Glu His Asn Val Glu Ser Ser Arg Trp Glu Pro Arg Arg Arg Gly 115 120 125

Ala Cys Gly Ser Arg Gly Gly Asn Phe Pro Ser Pro Arg Gly Gly Ser 130  $$135\$ 

Gly Val Ala Ser Leu Glu Arg Ala Glu Asn Ser Ser Thr Glu Pro Ala 145 155 160

Lys Ala Ile Lys Pro Ile Asp Arg Lys Ser Val His Gln Ile Cys Ser 165 170 175

Gly Pro Val Val Pro Ser Leu Arg Pro Asn Ala Val Lys Glu Leu Val

Glu Asn Ser Leu Asp Ala Gly Ala Thr Asn Val Asp Leu Lys Leu Lys

Asp Tyr Gly Val Asp Leu Ile Glu Val Ser Gly Asn Gly Cys Gly Val

Glu Glu Glu Asn Phe Glu Gly Phe Thr Leu Lys His His Thr Cys Lys 225 230 240

Ile Gln Glu Phe Ala Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg

Gly Glu Ala Leu Ser Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser 265 260 Thr Cys Arg Val Ser Ala Lys Val Gly Thr Arg Leu Val Phe Asp His Tyr Gly Lys Ile Ile Gln Lys Thr Pro Tyr Pro Arg Pro Arg Gly Met Thr Val Ser Val Lys Gln Leu Phe Ser Thr Leu Pro Val His His Lys 310 305 Glu Phe Gln Arg Asn Ile Lys Lys Lys Arg Ala Cys Phe Pro Phe Ala Phe Cys Arg Asp Cys Gln Phe Pro Glu Ala Ser Pro Ala Met Leu Pro 345 Val Gln Pro Val Glu Leu Thr Pro Arg Ser Thr Pro Pro His Pro Cys 355 Ser Leu Glu Asp Asn Val Ile Thr Val Phe Ser Ser Val Lys Asn Gly 380 370

Pro Gly Ser Ser Arg

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Pro 65	Pro	Arg	Pro	Leu	Gly 70	Ser	Arg	Gly	Ala	Glu 75	Ala	Ala	Glu	Pro	Gln 80
Glu	Gly	Leu	Ser	Ala 85	Thr	Val	Ser	Ala	Cys 90	Phe	Gln	Glu	Gln	Gln 95	Glu
Met	Asn	Thr	Leu 100	Gln	Gly	Pro	Val	Ser 105	Phe	Lys	Asp	Val	Ala 110	Val	Asp
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Tyr	Gly 130	Asp	Val	Met	Leu	Glu 135	Asn	Tyr	Ser	His	Leu 140	Val	Ser	Val	Gly
Tyr 145	Asp	Tyr	His	Gln	Ala 150	Lys	His	His	His	Gly 155	Val	Glu	Val	Lys	Glu 160
Val	Glu	Gln	Gly	Glu 165	Glu	Pro	Trp	Ile	Met 170	Glu	Gly	Glu	Phe	Pro 175	Cys
Gln	His	Ser	Pro 180	Glu	Pro	Ala	Lys	Ala 185	Ile	Lys	Pro	Ile	Asp 190	Arg	Lys
Ser	Val	His 195	Gln	Ile	Cys	Ser	Gly 200	Pro	Val	Val	Leu	Ser 205	Leu	Ser	Thr

720 780 795 Ala Val Lys Glu Leu Val Glu Asn Ser Leu Asp Ala Gly Ala Thr Asn 210 215 220

Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp Leu Ile Glu Val Ser 225 230 235 240

Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe Glu Gly Leu Ile Ser  $245 \hspace{1.5cm} 250 \hspace{1.5cm} 255 \hspace{1.5cm}$ 

Phe Ser Ser Glu Thr Ser His Met 260